Claims 2 and 9-15 remain in prosecution. Claims 2 and 9-15 stand rejected. Claims 9 and 12 are herein amended.

Enclosed herewith is a clean version of the amended claims pursuant to 37 C.F.R. §1.121 *et seq.*

Claims 2, 9-11 and 13 are rejected pursuant to 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Claim 9 has been amended to obviate the indefiniteness rejections.

Claims 2, 9-12 and 14 are rejected pursuant to 35 U.S.C. §103 as being obvious in view of Tarcha et al. (U.S. Pat. No. 5,266,498) and Nelson et al. (U.S. Pat. No. 4,487,198). Claims 13 and 15 are rejected pursuant to 35 U.S.C. §103 as being obvious in view Tarcha et al., Nelson et al. and Muller (U.S. Pat. No. 5,126,244). Tarcha et al. teaches an assay for an analyte in a test sample that uses a ligand binding reactons between the analyte and a specific binding member pair having a Raman active reporter. However, as admitted by the Examiner, Tarcha does not teach the irradiation of the specific binding member pair having a Raman active reporter with light having a wavelength within the claimed range of the Applicant's claimed method and/or system.

Claims 13 and 15 are rejected pursuant to 35 U.S.C. §103 as being obvious in view Nelson et al., Herron et al. (U.S. Pat. No. 5,512,492) and Muller. Muller has been cited to show the use of *E.coli* antibodies in an immunoassay is known in the art.

Claims 13 and 15 are rejected pursuant to 35 U.S.C. §103 as being obvious in view of Chadha et al., Herron et al. and Muller et al.

Claims 2, 9-12 and 14 are rejected pursuant to 35 U.S.C. §103 as being obvious in view of Nelson et al. and Herron et al. Herron et al. teaches a method and apparatus for evanescent fluoroimmunassays. The Examiner states that because Herron et al. teaches the use of excess antibodies to increase the sensitivity of the fluoroimmunassays, one of ordinary skill in the art would have expected that the use of excess antibodies to increase the sensitivity of Applicant's claimed method and/or system, i.e. the resonance Raman spectra emitted from the excess, or any, irradiated antibodies would not have interfered with the resonance Raman spectra emitted from the irradiated microorganisms.

Herron et al. does not relate to Raman spectroscopy. Herron et al. relates to fluoroimmunoassays. In Herron et al., immobilized capture molecules are positioned along a waveguide. Antibodies bound to a tracer molecule and molecules of a selected analyte having a binding affinity to the antibodies are placed in a sample and flowed through the waveguide. Bound molecule /tracer molecule/anitboidy complexes form and attach to the immobilized capture molecules. The complexes are excited with evanescent light and the tracer molecules of the complexes fluoresce. Due to the proximity of the bound complexes to the surface of the waveguide probe and a means for sensing the fluorescent light, the unbound tracer molecules, being positioned away from the surface of the waveguide probe, are not excited by the evanescent light and, therefore, do not fluoresce. Accordingly, an excess of antibodies bound to tracer molecules can be used without comprising the sensitivity of the fluoroimmunoassay.

The resonance Raman spectra of irradiating an antibody is not discussed, nor is it relevant, to the teachings of Heron et al. In summation, the principles of detection set forth in Heron et al. and relied upon the Examiner to prove that one of skill in the art would have expected that the use of an excess of antibodies to increase the sensitivity of the claimed method

and/or system are inapposite to the principles of detection used and applied in the claimed method and/or system.

The Examiner has rejected claims 2 and 9-12 pursuant to 35 U.S.C. §103 as being obvious in view of Chadha et al. in view of Herron et al.

Enclosed herewith is a declaration ("Declaration") submitted pursuant to 37 C.F.R. §1.132. The Declaration sets forth facts which evidence that the claimed method and system for detecting the presence of a specific microorganism in a sample yields unexpected results in view of the cited prior art. As set forth in paragraph 6 of the Declaration, it was known to those of skill in the art that the irradiation of aromatic amino acids with light having a wavelength **within the claimed range** [emphasis added] produced resonance Raman spectra. The resonance Raman spectra emitted from the aromatic amino acids created an expectation to those of skill in the art that the irradiation of antibody, i.e. a molecule comprised of aromatic amino acids, and/or antibody-antigen complexes with light having a wavelength **within the claimed range** [emphasis added] would have produced resonance Raman spectra that would have interfered with the resonance Raman spectra of microorganisms to be detected in an assay utilizing resonance Raman spectroscopy. See paragraphs 6-8 of the Declaration. Accordingly, one of skill in the art would not combine the primary references, i.e. Tarcha et al., Nelson et al., and Chadha et al., with any of the secondary references because one of skill in the art would expect the emitted resonance Raman spectra of the antibodies that had been irradiated with light **within the claimed range** [emphasis added] to render the claimed method and/or system ineffective. In fact, the use of antibodies in the claimed method and/or system was unexpectedly effective and yielded the unexpected result of providing the claimed method and/or system wherein the ratio of antibody to microorganisms in the sample is at least 200:1. Accordingly, it is respectfully

submitted that the Examiner's obviousness rejections in view of the cited prior art have been obviated in view of the arguments discussed *supra* and the Declaration.

If the Examiner believes that a telephonic interview Applicant's representative would further the prosecution of the application, the Examiner is cordially invited to contact Applicant's representative at the telephone number listed below.

It is respectfully submitted that the claims are now in condition for allowance and the same is earnestly solicited.

Respectfully submitted

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9. (Thrice Amended) A method for detecting the presence of a specific microorganism in a sample, said microorganism having a characteristic resonance enhanced Raman backscattered energy spectrum produced by irradiating nucleic acids in said microorganisms at a wavelength between 242-257 nm, comprising:

(a) contacting said sample with a medium comprising solid phase immobilized antibodies which specifically bind to a characteristic cell surface antigen on said microorganism to form an antigen-antibody complex, thereby immobilizing said microorganism on said solid phase;

(b) irradiating the solid phase of step (a) with a laser light of 242-257 nm to produce a resonance enhanced Raman backscattered energy, said antibodies emitting essentially no resonance Raman spectra that interfere with the resonance Raman spectra of said microorganism; and

(c) comparing said induced spectrum of step (b) with said characteristic spectrum to detect the presence of said microorganism in said sample, the sample having at least 200 fold immobilized antibodies in excess of target antigen.

12. (Twice Amended) A system for the detecting the presence of a specific microorganism in a sample, said microorganism having a characteristic resonance enhanced Raman backscattered energy spectrum produced by irradiating nucleic acids in said microorganisms at a wavelength between 242-257 nm, comprising:

(a) means for contacting said sample with a medium comprising solid phase immobilized antibodies which specifically bind to a characteristic cell surface antigen on said microorganism to form an antigen-antibody complex, thereby immobilizing said microorganism on said solid phase, the solid phase antibodies being at least 200 fold in excess of antigen, the antibodies emitting essentially no resonance Raman spectra that interfere with the resonance Raman spectra of said microorganism when irradiated with a laser light of 242-257 nm ;

(b) means for irradiating the solid phase of step (a) with a laser light of 242-257 nm to produce a resonance enhanced Raman backscattered energy spectrum; and

(c) means for comparing said induced spectrum of step (b) with said characteristic spectrum to detect the presence of said microorganism in said sample.